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Refining Decisions for Identifying Primary Care Patients Who Require A Work-Up for Glaucoma: Intraocular Pressure Changes with Central Corneal Thickness

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Abstract

PURPOSE
The factors associated with the increased risk of glaucoma include intraocular pressure (IOP), central corneal thickness (CCT), vertical cup-to-disc ratio, visual field index, age, and diabetes mellitus. We have investigated the relation of IOP with CCT in normal, healthy pre-presbyopic persons.

METHODS
A total population of 698 normal patients (1396 eyes), aged 4 to 40 years, were evaluated in two separate clinics, one in Houston, Texas, USA and the second in Oakville, Ontario, Canada. IOP was measured using a noncontact tonometry (NCT 20 Topcon). In Houston, CCT was determined by using the Pentacam (Occulus Pentacam – Belinea) and an optical pachymetry that utilized optical low-coherence reflectometry (OLCR) technology, and in Oakville, a Hagg-Streit slit lamp–mounted pachymeter was used.

RESULTS
Of the total number of eyes tested, 1226 eyes had IOP of 21 millimetres of mercury (mm Hg) or lower and 134 eyes had IOP greater than 21 mm Hg. For the normal IOP group (n = 1226 eyes), the overall IOP mean was 15.63 +/– 2.87 mm Hg; the overall CCT mean was 550.21 +/– 39.64 micrometres (µm). In the normal IOP group, for every 10 µm change in CCT, IOP changed a statistically significant amount of 2.49 mm Hg (p <0.05 to <0.001), except for the 10 nm CCT bins above and below the 550 µm mean.

CONCLUSIONS
Although many investigators have described a positive correlation between IOP and CCT, this relationship has not been demonstrated in normal, healthy pre-presbyopic persons. There is a significant change of IOP with CCT (2.49 mm Hg IOP change per 100 µm of CCT). These normative data allow primary eye care clinicians to accurately determine normal and abnormal IOP and refine the index of suspicion for identifying patients who need to be worked up for glaucoma.

KEY WORDS:
central cornea thickness, intraocular pressure, noncontact tonometry, glaucoma

Sommaire

BUT

Les facteurs associés à un risque accru de glaucome comprennent la pression intraoculaire (PIO), l'épaisseur cornéenne centrale (ECC), le rapport cup/disc vertical, le relevé de champ visuel, l'âge et le diabète sucré. On a étudié la relation entre la PIO et l'ECC chez des personnes normales et en bonne santé ayant une prépresbytie.

MÉTHODES

On a évalué un nombre total de 698 patients normaux (1 396 yeux), âgés de 4 à 40 ans, dans deux cliniques distinctes : l'une à Houston, au Texas, aux États Unis, l'autre à Oakville, en Ontario, au Canada. On a mesuré la PIO à l'aide d'un tonomètre sans contact (NCT 20 de Topcon). À Houston, on a déterminé l'ECC au moyen d'une Pentacam (Pentacam d'Occulus – Belinea) et d'un pachymètre optique ayant recours à la technologie de la réflectométrie à faible cohérence optique (RFCO); à Oakville, on a utilisé un pachymètre avec lampe à fente de Hagg Streit.

RÉSULTATS

Parmi tous les yeux examinés, 1 226 yeux présentaient une PIO de 21 millimètres de mercure (mm Hg) ou moins, et 134 yeux avaient une PIO supérieure à 21 mm Hg. Pour le groupe ayant une PIO normale (n = 1 226 yeux), la moyenne de la PIO globale était de 15,63 mm Hg, ± 2,87 mm Hg. La moyenne de l'ECC globale était de 550,21 micromètres (µm), ± 39,64 ×m. Dans le groupe ayant une PIO normale, pour chaque variation de 10 nanomètres (nm) de l'ECC, la PIO changeait d'une quantité statistiquement significative, à savoir 0,249 µm (p <0,05 à <0,001), sauf pour les compartiments de l'ECC de 10 nm inférieurs ou supérieurs à la moyenne de 550 µm.

CONCLUSION

De nombreux chercheurs ont décrit une corrélation positive entre la PIO et l'ECC, mais cette relation n'a pas été démontrée chez des personnes normales en bonne santé ayant une prépresbytie. Il existe une variation significative de la PIO en fonction de l'ECC (variation de la PIO de 2,49 mm Hg par 100 µm d'ECC). Ces données normatives permettent aux techniciens en soins oculovisuels primaires de déterminer une PIO normale et anormale et d'affiner l'indice de suspicion servant à identifier les patients devant faire l'objet d'analyses concernant un glaucome. être personnalisées. Une seule étude, comme AREDS 2, bien que très importante, ne peut déterminer à elle-seule le comportement clinique des professionnels de la vue. L'importance du suivi régulier du patient doit également être comprise par tous.

Many investigators have described a positive correlation between IOP and CCT.[1-23] Others have provided a CCT-correction factor for IOP; taking all of the data of these studies together, the average correction factor for IOP is 2.6 mm Hg per 100 ×m CCT with a range of 0.0 to 6.3 mm Hg.[4,9,24-34] See **Table 1**.

Although the relationship between IOP and CCT has been studied in various populations, a wide range of IOP cases have not been investigated in large numbers of normal healthy pre-presbyopic subjects in North America (USA and Canada) using standard clinical screening measures of IOP (non-contact tonometry or NCT). What is not well delineated is an answer to a general research question: Can the index of suspicion for identifying primary care patients who require a workup for glaucoma be refined by determining a CCT-corrected IOP measured by NCT?

Table 1. *Studies Quantifying the Relationship between Intraocular Pressure (IOP) and Central Corneal Thickness (CCT)*

STUDY		SUBJECTS		METHODOLOGY and RESULTS						CLINICAL GUIDELINE
Year	**Author(s)**	**Eyes**	**Other**	**Tonometry (mm Hg)**			**Pachymetry - Central Corneal Thickness (µm)**			**IOP change per 100 nm change in CCT**
		(n)		***Type***	***(mean)***	***(sd)***	***Type***	***(mean)***	***(sd)***	***(mm Hg per 100 nm)***
1975	Elhers et al[32]	29	Normal cornea; no edema; intraocular cataract or glaucoma surgery	Goldmann applanation	n/a	n/a	Optical: Hagg-Streit slit lamp-mounted	n/a	n/a	6.3
1978	Johnson et al[33]	2	One (1) 17-year-old female; normal cornea	Cannulated* Perkins applanation Schiotz applanation	11.0 35.0 34.0	n/a	n/a	900	n/a	5.0
1993	Whitacre et al[34]	15	Normal cornea; intraocular cataract, glaucoma or victrectomy surgeries	Perkins applanation simultaneous with manometry controlled IOP's of 10, 20 & 30 mm Hg	n/a	n/a	Optical: Hagg-Streit slit lamp-mounted or ultrasound: Topcon	n/a	n/a	2.5
1997	Wolfs et al[12]	Age 55 yr. or older 352 13 30	>55 yr; normal cornea; eye surgery >12 months ago Control Ocular hypertensive Primary open angle glaucoma	Goldmann applanation (assumed)	14.6 18.7 14.3	n/a n/a n/a	Ultrasound	537.4 553.4 515.9	n/a n/a n/a	1.9
1998	Foster et al[17]	2456	Ages 10 to 87 yr.; East Asian Mongolian population	Goldmann applanation	12.7	3.4	Optical: Hagg-Streit slit lamp-mounted	504.5	32	2.1

Table 1 continued

Studies Quantifying the Relationship Between Intraocular Pressure and Central Corneal Thickness

STUDY		SUBJECTS		METHODOLOGY and RESULTS						CLINICAL GUIDELINE
Year	**Author(s)**	**Eyes**	**Other**	**Tonometry (mm Hg)**			**Pachymetry - Central Corneal Thickness (µm)**			**IOP change per 100 nm change in CCT**
		(n)		***Type***	***(mean)***	***(sd)***	***Type***	***(mean)***	***(sd)***	***(mm Hg per 100 nm)***
2001	Feltgen et al[35]	73	Intraocular glaucoma or retinal surgery; ages 13 to 88 yrs., mean = 40.7	Intracameral cannula Perkins applanation Tono-Pen	19.5 17.5 18.7	6.5 6.5 7.2	Ultrasound	580	54	0.0
2001	Singh et al[36]	23 41 10 13	Control Ocular hypertensive Normal pressure glaucoma Primary open angle glaucoma	Goldmann applanation/ pneumotonometry	15.7 / 14.1 24.6/ 20.5 15.7/ 14.9 27.5/ 22.8	1.8/ 2.3 2.1/2.9 2.9/2.7 5.1/5.0	Ultrasound	554 570 538 547	32 32 51 34	2.0
2002	Bhan et al[37]	181	Normal cornea	Tono-pen Goldmann applanation Ocular Blood Flow (OBF) pneumotonometry	14.7 14.4 16.4	5.0 4.9 6.4	Ultrasound	551	49	1.0 2.3 2.8
2002	Doughty et al[38]	104 75 91	Normal cornea; European; ages 5 to 15 yr. Normal cornea; European; ages 32 to 60 yr. Normal cornea; European; ages 61 to 82 yr.	Noncontact Perkins applanation Perkins applanation	16.7 13.0 13.6	2.9 3.5 2.5	Ultrasound & specular microscopy Specular microscope Ultrasound	529 533 527	34 33 34	2.5 1.9 4.9

Table 1 continued										
Studies Quantifying the Relationship Between Intraocular Pressure and Central Corneal Thickness										
STUDY		**SUBJECTS**		**METHODOLOGY and RESULTS**						**CLINICAL GUIDELINE**
Year	**Author(s)**	**Eyes**	**Other**	**Tonometry (mm Hg)**			**Pachymetry - Central Corneal Thickness (µm)**			**IOP change per 100 nm change in CCT**
		(n)		***Type***	***(mean)***	***(sd)***	***Type***	***(mean)***	***(sd)***	***(mm Hg per 100 nm)***
2006	Kohlhaas et al[39]	125	Normal cornea; ages 18 to 91 yr, mean = 72.9 + 13.2; cataract surgery; masked, prospective clinical trial	Perkins applanation simultaneous with manometry controlled IOPs of 20, 35 and 50 mm Hg	n/a	n/a	Ultrasound	569	44	4.0
2011	Heidary et al[40]	180	Normal cornea; ages 8 to 16 yr.; Malay population	Noncontact	15.7	3.1	Specular microscope	530.9	31	3.5
2012	Sakalar et al[41]	30,320	Normal cornea; ages 8 to 16 yr.; Turkish population	Noncontact	14.2	2.9	Ultrasound	558.3	34	0.2
2012	Fern et al[42]	670	Normal cornea; ages 17 to 22 yr.; The COMET Study Group	Goldmann applanation	15.1	0.1 SE	Ultrasound	562.4	1.8 SE	2.0
										Average = 2.6

*Cannulated tonometry means cannulation of anterior chamber of eye and manometric determination of intraocular pressure (IOP).
OHT - ocular hypertensive subject
POAG - primary open-angle glaucoma
SE- standard error

This question is important because in general, the most commonly used screening measure of IOP is the NCT. In a population-based prevalence survey of more than 5000 individuals aged 40 years and over, participants who had a screening IOP greater than 30 mm Hg were over 38 times more likely to have glaucoma (as defined in the study) compared with individuals with an IOP below 15 mm Hg.[35] In the Blue Mountains Eye Study, the odds of developing glaucoma were four to seven times higher when the screening IOP was greater than 21 mm Hg than in those with lower IOP.[36] Further, the chances of developing glaucoma is two to eight times higher in patients with IOP asymmetry between eyes greater than 3 mm Hg than in patients with smaller or no intraocular pressure asymmetry.[37] Thus, although the level of IOP is directly related to the probability of glaucomatous visual field loss, it is not currently known how the use of the screening NCT relates to CCT.

Further, research indicates that CCT-corrected IOP formula seems to oversimplify the relationship of a “true” IOP based on pachymetry measurement. Currently, CCT results are commonly classified as thin, average, or thick.[38] The Ocular Hypertensive Treatment Study (OHTS) showed that CCT was a significant predictor of which patients with ocular hypertension are at higher risk for converting to glaucoma (eyes with CCT of 555 µm or less had a threefold greater risk of developing glaucoma compared with eyes that had CCT of more than 588 µm).[18]

In a study using CCT-corrected IOP, the OHTS prediction model did not perform better than the original model (without the CCT-corrected IOP), and analysis showed that CCT continued to be a statistically significant predictor in the multivariate model (**Table 2**).[39] CCT is a predictor of ocular hypertension converting to glaucoma, which is not fully explained by a CCT-corrected IOP adjustment. CCT is not to be considered a true independent risk factor for glaucoma.[40]

The validity of CCT-corrected IOP is based on the accuracy and precision of these measurements. Accuracy is the degree of closeness of a measured quantity to its true value. Precision (reproducibility or repeatability), which is closely related to accuracy, is the degree to which repeated measurements show similar results.[41]

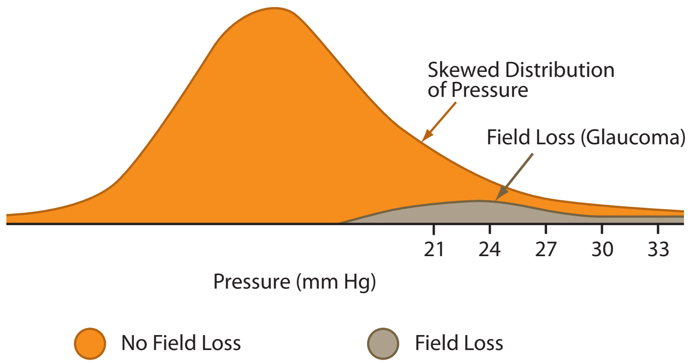
The cornea, which is the most anterior tissue of the eye, is a transparent curved tissue, which vaults over the iris, pupil, and anterior chamber.[42] The cornea refracts light with the crystalline lens to focus images on the retina; the cornea accounts for approximately two-thirds of the eye's

Table 2. *Central Corneal Thickness (CCT) Groups with Mean IOP and Statistical Analysis for the Normal IOP Group (7 – 20 mm Hg)*

Row	*Number of Eyes*	*Range CCT (µm)*	*CCT Group*	*Mean IOP (mm Hg)*	*SD*	*Standard Error of the Mean*	*t-value*	*Significance (p)*	*Degrees of Freedom (df)*
1[c]	9	359–454	n/a	n/a	n/a	n/a	n/a	n/a	n/a
2[b]	8	455–464	460	12.75	3.01	1.06	2.56	<0.01	113
3[b]	8	465–474	470	13.13	3.72	1.32	1.81	<0.05	113
4	23	475–484	480	14.15	2.17	0.45	2.71	<0.01	128
5	34	485–494	490	12.68	2.73	0.47	5.41	<0.001	139
6	62	495–504	500	14.77	2.77	0.35	1.81	<0.05	167
7	62	505–514	510	14.44	2.77	0.35	2.57	<0.02	167
8	116	515–524	520	14.42	2.24	0.21	3.48	<0.001	221
9	114	525–534	530	14.84	3.13	0.29	1.84	<0.05	219
10	112	535–544	540	15.43	2.94	0.28	0.32	>0.5	217
11[a]	107	545–554	550	15.55	2.58	0.25	0.00	>0.5	212
12	136	555–564	560	16.07	2.69	0.23	–1.53	>0.05	241
13	109	565–574	570	16.23	2.38	0.23	–2.01	<0.05	214
14	103	575–584	580	16.85	2.48	0.24	–3.72	<0.001	208
15	77	585–594	590	17.04	2.46	0.28	–3.97	<0.001	182
16	45	595–604	600	16.43	2.71	0.40	–1.85	<0.05	150
17	29	605–614	610	16.83	2.88	0.53	–2.17	<0.05	134
18	26	615–624	620	17.63	2.26	0.44	–4.09	<0.001	131
19[b]	17	625–634	630	18.00	2.32	0.56	–3.98	<0.001	122
20[b]	13	635–644	640	18.36	1.84	0.51	–4.95	<0.001	118
21[b]	7	645–654	650	17.21	2.38	0.90	–1.78	<0.05	112
22[c]	9	655–701	n/a	n/a	n/a	n/a	n/a	n/a	n/a
Total = 1226									

[a]Mean CCT group
[b]CCT groups with less than 20 eyes
[c]CCT groups with less than 7 or no eyes

Figure 1. *In this diagram of intraocular pressure distribution there is a visible skew toward higher pressures (exaggerated slightly compared to the actual distribution). The average pressure among those with glaucomatous visual field loss is in the low 20s, even though glaucoma is not present in most individuals with similar pressures. And, although it is not common, some individuals with pressures in the upper teens have glaucomatous visual field loss.*



total optical power.[43] The adult CCT of approximately 540 µm is reached by the age of 3 years[1,2] and remains stable throughout life.[3,44] The accuracy and precision of CCT measurement vary slightly with different instruments.[45-52]

IOP is the fluid pressure in the eye measured in millimetres of mercury. IOP is mainly determined by the coupling of the production of aqueous humour from the eye's ciliary body and its drainage through the anterior chamber angle, specifically the trabecular meshwork and Schlemm's canal. The normal range for IOP is 10 to 21 mm Hg, with a mean of 15.5 mm Hg.[53] Clinically, IOP is measured with a Goldmann applanation tonometer or, more commonly, its derived successor, the noncontact (air-puff) tonometer (NCT). Corneal thickness and rigidity influence IOP, according to the Imbert-Fick law. This law states that the force to applanate the anterior corneal surface is equal to the true IOP times the applanated area at the posterior corneal surface, assuming the cornea is 520 µm thick.[54,55] Corneal indentation produced by a fixed force depends on many factors, including CTT, elasticity, and viscoelasticity, as well as other structural and physiological properties of the cornea. IOP is maintained throughout life. It is similar between the genders, and diurnal and some seasonal variations may exist.[56] The IOP distribution in the general population is not a normal Gaussian distribution but is skewed toward higher pressures, where an associated increase in visual field loss is often present (**Figure 1**).[57] IOP measurement has been shown to be accurate and precise with a number of instruments, including NCT, which may be used as a screening device for IOP measurement.[58-64]

The challenge is investigating IOP with the use of screening devices available in a primary eye care setting (NCT) and determining the relationship between IOP and CCT in normal healthy pre-presbyopic persons.

Taken together, answers to our specific research question—is there a difference in intraocular pressure, as measured with a screening NCT, with varying central corneal thickness in a normal healthy pre-presbyopic population?—and our research objective—to provide data for young normal patients, gathered using screening IOP measuring devices available in a primary eye care setting (NCT), which delineate the relationship between IOP and CCT—will allow routine clinical measures to refine the index of suspicion for identifying primary care patients who require a workup for glaucoma.

METHODS

In the Houston–Oakville study, a total of 698 normal healthy pre-presbyopic patients (1396 eyes) were evaluated in two separate clinics located in Houston, Texas (USA) and Oakville, Ontario (Canada). After written informed consent was obtained, data collected included each patient's age, race (by self-report), gender, date of birth, IOP, and CCT.

In Houston, consecutive patients were included from the date of study onset. In Oakville, patients were selected on the basis of willingness to undergo the Optos examination. Young normal subjects aged 4 to 40 years were included. Patients aged 4 years or less (due to lack of cooperation) and those over age 41 years (who were more at risk for glaucoma due to their age) were excluded. Data from a few patients were not included due to inability to procure accurate anterior segment assessment with the Pentacam. Patients with glaucoma (visual field defects, visible optic disc damage, or nerve fiber layer thinning) and those who had undergone Lasik or corneal transplant surgeries were also excluded.

Intraocular Pressure

NCT, with the Topcon CT-20 auto-NCT, was performed on all patients, at both clinics in the United States and Canada. NCT utilizes an applanation tonometer, which works on the principle of a time interval. It determines IOP by measuring the time in milliseconds from the initial generation of the puff of air to the time when the cornea is flattened exactly to the point where the timing device stops. Patients with all IOP levels were included. NCT use allowed the findings of this study to be generalized to routine clinical vision care.

Central Corneal Thickness

In Houston, the Pentacam (Occulus Pentacam – Belinea) was used for every patient to determine CCT. The Pentacam is an instrument that uses a rotating Scheimpflug camera to take multiple images of the anterior segment. The centre of the cornea is precisely measured with this rotational imaging process. Measurements take less than 2-seconds apart, and minute eye movements are captured and simultaneously corrected. Images are analyzed by a computer to generate three-dimensional images and calculate the measurements of the eye, including corneal topography, corneal thickness, AC depth, volume, angle, and pupil diameter. In Oakville, a Hagg-Streit slit-lamp mounted optical-pachymeter was used to determine corneal thickness; the Hagg-Streit optical-pachymeter utilizes OLCR (optical low-coherence reflectometry) technology.

RESULTS

From the Houston–Oakville study capture of 698 patients (1396 eyes), complete data were obtained to evaluate 1360 eyes. Of those 1360 eyes, 1226 eyes had normal IOP (range 7–21 mm Hg), with 514 eyes of male subjects (*n* = 257, average age 17.01 +/– 16.3, range 5–40) and 712 eyes of female subjects (*n* = 356; average age 20.61 +/– 9.65, range 4–39).

Of the 1360 eyes with complete data:
- Average IOP equalled 16.05 +/– 3.31 mm Hg
- Average CCT equalled 551.75 +/– 40.26 µm

Of the 1226 eyes with normal IOP (range 7–21 mm Hg):
- Average IOP equalled 15.63 +/– 2.87 mm Hg
- Average CCT equalled 550.21 +/– 39.64 µm

Of the 134 eyes with high IOP (>21 mm Hg):
- Average IOP equalled 22.48 +/– 3.13 mm Hg
- Average CCT equalled 583.75 +/– 43.49 µm.

For the 1360 eyes with complete data, IOP increased with increased CCT as seen in the scatter plot of **Figure 2**. The R-squared value is 0.158, which indicates that about 16% of the variance in measured IOP is associated with changes in CCT and that the other 84% of the variance is attributable to other factors (race, age, idiopathic, etc.). The slope of the scatter plot in **Figure 2** is the correlation coefficient R, which is 0.397; this indicates that measured IOP and CCT are mildly correlated.

Figure 2. *For our young normal pre-presbyopic population (n = 1360 eyes) this figure shows the scatter plot of intraocular pressure (IOP) versus central corneal thickness (CCT) measurements. The slope of the scatter plot is the correlation coefficient r which is 0.397; this indicates that the measured IOP and CCT are mildly correlated. The square of the correlation coefficient (r^2=0.158) indicates the percentage of variance in IOP that can be accounted for by knowing the CCT; that is, about 16% of the variance in measured IOP is associated with changes in CCT and the other 84% of the variance is attributable to the other factors (race, age, idiopathic, etc).*

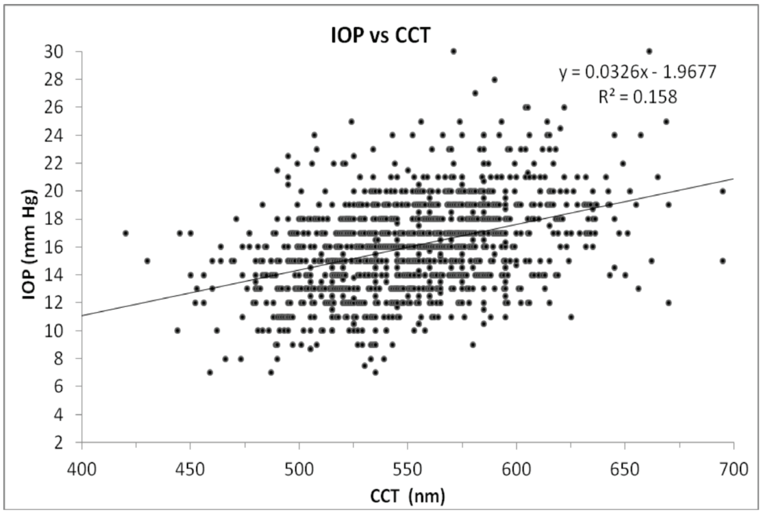


Table 3. *Intraocular Pressure Increases with an Increase in Central Corneal Thickness*

CCT Group	Rows from Table 2	CCT Range	Change in IOP	Change in IOP per 100 nm change in CCT
480 to 620	4 to 18	140	3.48	2.49
460 to 650	2 to 21	190	4.46	2.35

Figure 3. *For our young normal pre-presbyopic population (n = 1360 eyes), 1226 eyes had normal intraocluar pressure (IOP equal or less than 21 mm Hg) which are included in this plot. The graph shows the average IOP (mm Hg) for each of the CCT-groups and corresponding standard deviation (SD) bars (+/-1 SD). See Table 2 for supporting data.*

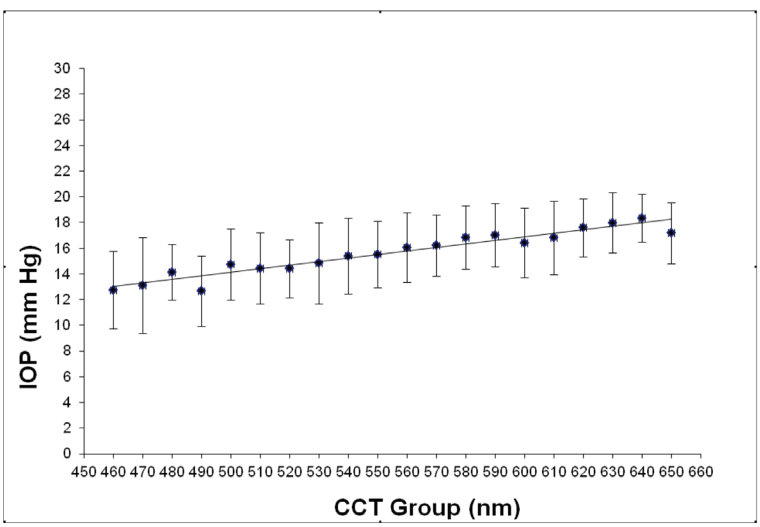


Table 4a. *Young Adult Data*

Young Normal (IOP ≤21)			High IOP* (IOP >21)		Asian (IOP ≤21)		Black (IOP ≤21)		Hispanic (IOP ≤21)		Other (Pakistani and Indian Descent) (IOP ≤21)		Caucasian (IOP ≤21)	
N =	Total	613	Total	81	Total	36	Total	178	Total	151	Total	82	Total	166
	Male	257	Male	31	Male	19	Male	62	Male	71	Male	34	Male	71
	Female	356	Female	50	Female	17	Female	116	Female	80	Female	48	Female	96
Eyes *N* =		**1226**		**134**		**72**		**356**		**302**		**164**		**332**
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age	18.81	12.98	13.63	5.52	21.28	9.96	19.03	9.56	17.59	8.90	16.82	8.33	21.18	9.62
Intraocular pressure (IOP)	15.63	2.87	22.48	3.13	15.09	2.61	15.66	2.93	16.23	2.81	15.99	2.99	15.13	2.98
Central Corneal thickness (CCT)	550.21	39.64	583.75	42.49	550.64	34.59	537.36	37.81	560.61	39.85	553.25	37.45	553.51	39.20

*Included in the high IOP group are 1 Asian, 18 Black, 20 Hispanic, 35 Other, and 7 Caucasian who are not included in the respective Ethnicity columns.

Table 4b. *t-Test Comparison*

Race	IOP	CCT
CxO	0.02	
CxH	0.001	
CxB		0.001
CxA		
CxOverAll		
OxH		
OxB		0.001
OxA		
HxB		0.001
HxA	0.02	
BxA		0.05

High IOP versus Normal IOP

IOP	CCT
	0.01
	Thicker

High IOP thicker cornea

Figure 3 was derived by selecting those eyes (n = 1226) with normal IOP (7–21 mm Hg) and then averaging the IOP for various CCT ranges or CCT groups. For example, the CCT group of 510 µm, IOP values of eyes (n = 62) with corneal thickness ranges from 505 to 514 µm were averaged; for the CCT group of 520 µm, IOP values of eyes (n = 116) with corneal thickness ranges from 515 to 524 µm were averaged. The mean IOP of each CCT group above or below the mean CCT group of 550 µm was significantly different at the 0.05 level. **Table 3** summarizes the change in IOP over a range of CCT measurements from the data in **Table 2**. For rows 4 to 18, which correspond to CCT groups 480 to 620 µm with 20 or more eyes, the change in IOP over the 140-µm CCT range was 3.48 mm Hg, hence a 2.49-mm Hg change per 100 µm of CCT. For rows 2 to 21, which correspond to CCT groups 440 to 650 µm with seven or more eyes, the change in IOP over the 190-µm CCT range was 4.46 mm Hg, hence a 2.35 mm Hg change in IOP per 100 µm of CCT.

Several parameters were different in the comparison of the various groups (see **Table 4**).

At the 0.02 level or higher:
- Asian (15.09 +/− 2.61 mm Hg) patients had lower measured IOP than Caucasian (15.13 +/− 2.98 mm Hg) or Hispanic patients (16.23 +/− 2.81 mm Hg).
- Caucasian (15.13 +/− 2.98 mm Hg) patients had lower measured IOP than Hispanic (16.23 +/− 2.81 mm Hg) patients.

At the 0.01 level or higher:
- Female (546.92 +/− 38.26 µm) patients had thinner CCT than male (555.01 +/− 40.55 µm) patients.
- The high IOP (>21 mm Hg) group had thicker CCT (583.75 +/− 42.49 µm) than the normal IOP group (555.21 +/− 39.64 µm).

At the 0.001 level or higher:
- Black patients had thinner CCT (537.36 +/− 37.81 µm) than other groups (except Asians $p = 0.05$). The overall average of central corneal thickness was 550.21 +/− 39.64 µm.

Between-site measures were generally not significantly different. Although IOP was lower overall in Canada (14.81 +/− 3.09 versus 15.85 +/− 2.85 mm Hg), this difference was not statistically significant when comparing Caucasian patients from Canada and the United States (14.81 +/− 3.09 versus 15.13 +/− 2.98 mm Hg).

DISCUSSION

The clinical dilemma is that accurate assessment of IOP is important for patients who might have glaucoma (assessing the index of suspicion) and is very important for those who are being treated for glaucoma. How then, is the clinician to judge the IOP accurately in the presence of varying ranges of corneal thickness? In the Houston–Oakville study, the average:

- IOP equalled 15.63 +/− 2.87 mm Hg
- CCT equalled 550.21 +/− 39.64 µm.

Each of these findings has been related to glaucoma incidence, progression, or both, but it is difficult to determine how important a given IOP finding is without knowing the CCT for a given patient.[5,12,18]

Accepting this premise makes it important to know how IOP and CCT are related. The answer to the specific research question helps identify the correction factor that might be used. The influence of CCT on measured IOP[24,25] was reported as early as the 1970s; however, it is only now coming into mainstream clinical care, facilitated by new technology. Using routinely available clinical equipment (CCT measures) allows the general clinician to implement corrections and bring research into clinical care immediately.

Study Limitations

The Houston–Oakville study limitations include the method of tonometry used. Further, the study was limited to persons living at just two sites, and it may not be possible to generalize the findings to persons of similar reported ancestry living elsewhere.

The gold standard for glaucoma care is Goldmann applanation tonometry. To facilitate gathering of data, the Houston–Oakville study group elected to use a Topcon CT-20 auto-NCT. NCT is a frequently used clinical test for routine IOP examination in primary eye care offices. It is possible that there will be clinical differences in IOP measurements when NCT, rather than Goldmann tonometry, is used. However, Tonnu et al.[65] found moderate agreement between NCT (Topcon CT-80) and Goldmann applanation tonometry (mean difference of 0.7 mm Hg), and there was no significant difference between NCT (Canon TX-10) and Goldmann applanation tonometry, in either intrasession or intersession repeatability testing (two-tail *t*-test, $p > 0.075$; degree of freedom (df) = 119).[66] Furthermore, the relation between IOP and CCT is the important factor, not the absolute IOP reading.

The IOP assessment in the Houston–Oakville study was based on a single-average measure (average of two measurements taken consecutively within a 10-second time-frame) at various times throughout the day (9:00 a.m. to 7:00 p.m.). On the surface, this could be a concern, as there can be significant diurnal variations in IOP. Indeed, diurnal IOP fluctuation has been identified as an important risk factor for visual field deterioration in glaucoma.[56] A single IOP measure will seldom be used to establish a diagnosis or alter treatment for any form of glaucoma. However, the result of the Houston–Oakville study compares CCT and IOP, and possible fluctuation would not influence the structural interrelations identified; and the study averages IOP measured at different times of the day. So, the IOP measured in the study is a daylight average, which moderates the extreme readings of the diurnal range of IOP measured. That said, the diurnal variation in IOP (not observed in CCT except for post-sleep corneal edema secondary to hypoxia) adds measurement noise, reduces the relationship between IOP and CCT, and lowers the R-squared value. If all measurements were taken at the same time of the day, then a higher R-squared value might have been found.

Corneal Thickness

In the Houston–Oakville study, the female subjects had thinner corneas compared with the male subjects by 8.1 µm (546.92 +/– 38.26 µm versus 555.00 +/– 40.55 µm, respectively; $t = 2.503$, $p = 0.02$). This differs from the OHTS results, which showed that the male subjects had thinner corneas by 4.7 µm (575 +/– 38.6 µm versus 570.3 +/– 39.4 µm).[18] The etiology of this difference is unclear. The OHTS investigators suggested that the cornea thins slightly with age, and the subjects of the Houston–Oakville study were substantially younger compared with the subjects of the OHTS. Perhaps the corneal thickness difference of the Houston–Oakville subjects would ultimately "cross over" so that the males would have thinner corneas, as the OHTS investigators found. In any event, the OHTS investigators did not feel that these small differences were clinically significant for glaucoma management or for accurate determination of IOP and the data from the Houston–Oakville study suggest this as well.

Clinical Application

The results of the Houston–Oakville study shed further light on how measured IOP might be "corrected" on the basis of the measures of CCT. **Figure 3** was derived by averaging the IOP of 1226 eyes, with normal IOP (7–21 mm Hg) for 10 µm CCT groups between 460 µm and 650 µm. From **Table 3**, the CCT groups between 480 and 620 µm had 20 or more IOP measurements, and the average change of IOP per 100 µm of CCT was 2.49 mm Hg. For the CCT groups with CCT between 460 and 650 µm, which had seven or more IOP measurements, the average change of IOP per 100 µm of CCT was 2.35 mm Hg. The "correction" of 2.49 mm Hg for every 100-µm increase in corneal thickness corresponded well with previous results (2.6 mm Hg per 100 µm of CCT; average correction from Table 1). The best "correction" factor to be used is still debated, as is whether a linear factor is even appropriate (although in Figures 2 and 3, it appears that the factor is linear for the 460–650 µm CCT range studied). Nonetheless, correction factors derived from patient samples, such as in the Houston–Oakville study, provide clinicians with a useful estimate of the effects that corneal thickness variations from a normal range may have on the IOP measurement of a given patient.

CONCLUSION

Data from the Houston–Oakville study provide new insight into the relation between CCT and IOP in young, normal persons. Evaluating and relating IOP to CCT will help improve clinical care. Identification of patients with abnormal CCT will allow the clinician to more closely estimate the accuracy of IOP readings for these patients.

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